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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/737,908 | 12/15/2000 | Jason Hill | CUB-5 | 2440 |

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| EXAMINER | |
|---|---|
| LUKTON; DAVID | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/737,908 | HILL ET AL. | |
| | Examiner | Art Unit | |
| | David Lukton | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *3-31* is/are pending in the application.

4a) Of the above claim(s) *13-16 and 18-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-12 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to preliminary amendment (filed 9/24/04), claims 1 and 2 have been cancelled, and the following claims amended: 3-19, 22, 25, 26 and 29-31.

Applicants' election of Group 2 (claims 3-12 and 17) is acknowledged. Claims 13-16, 18-31 are withdrawn from consideration. Also acknowledged is the elected specie (compound 85, i.e., the first compound listed on page 50) for which the substituent variables correspond as follows:

R = $-NH-CO-(CH_2)_8-CH_3$

m = 0

B' = hydrogen

A' is "substituted alkyl", i.e., methyl that is substituted with N-methylimidazole

$R^2$ = $-CH_2-CO-C_6H_4-NH_2$

. . . .

This application contains at least one sequence disclosure that is encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §131 and 132.

See, for example, the sequence recited in claim 25

Applicant is given the time period set in this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

✧

Claim 3 and 4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of USP 6,794,490. Although the conflicting claims are not identical, they are not patentably distinct from each other. There is overlap of the claimed genera. [This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

. . . .

Claims 3 and 4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending application Serial No. 09/738742. Although the conflicting claims are not identical, they are not patentably distinct from each other. There is overlap of the claimed genera.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application . See 37 CFR 1.78(d)

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-12 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Each of claims 3 and 4 is drawn to a compound "having" the indicated formula. The term "having" can be viewed as being "open-ended", with an effect similar to that of the term "comprising". Accordingly, it is asserted that the scope is unduly broad in view of the enabling disclosure.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or

unpredictability of the art, and breadth of the claims. As it happens, structure/activity relationships of antibacterial compounds are unpredictable. Consider, for example, the following:

- Gavini ("Pyridazine N-oxides. III. Synthesis and in vitro antimicrobial properties of N-oxide derivatives based on tricyclic indeno[2,1- c]pyridazine and benzo[f]cinnoline systems", *Archiv der Pharmazie* **333** (10) 341-6, 2000) discloses the preparation and testing of a series of pyridazine N-oxides. With the exception of compounds 3a, 3b, 4b and 5b, the compounds "demonstrated no activity against bacteria" (page 342, col 2).

- Fudou ("Haliangicin, a novel antifungal metabolite produced by a marine myxobacterium. 1. Fermentation and biological characteristics", *Journal of Antibiotics* **54** (2) 149-52, 2001) discloses the isolation of haliangicin which is produced by a marine bacteria; the compound contains a conjugated tatraene moiety and exhibited no antibacterial activity.

- Juvvadi ("Structure-activity studies of normal and retro pig cecropin-melittin hybrids", *Journal of Peptide Research* **53** (3) 244-51, 1999) discloses the preparation and antibacterial activity of cecropin-melittin hybrid peptides. Also disclosed is that the "retro" analogs (the polarity of the amide bond reversed) lost antibacterial activity.

- Avrahami (*Biochemistry* **40** (42) 12591-603, 2001) studied the effects of amino acid substitutions on the antimicrobial activity of amphipathic antimicrobial peptides. Many of the compounds prepared lost antibacterial activity as a result of a single amino acid substitution. Although after-the-fact rationalizations were provided, the observed structure/ activity relationships could not have been predicted *a priori*.

- Goldman, R. C. (*FEMS Microbiology Letters* **183**(2), 209-214, 2000) discloses (sentence bridging pages 210-211) that removal of an amino acid from a vancomycin eliminates activity.

- Harris, Constance (*Journal of Antibiotics* **38**(1), 51-7, 1985) discloses that replacement of an asparagine residue in vancomycin with isoaspartic acid eliminates

activity.

These and other references disclose that there do exist compounds which exhibit no antibacterial activity, and many of these inactive compounds are structurally analogous to compounds that are active. The key point is that the factors which give rise to activity or inactivity are unknown in the art; and certainly the specification has made no attempt to discuss such factors. Accordingly, the skilled microbiologist cannot predict antibacterial activity merely by viewing a structure

It remains the case that "undue experimentation" would be required to determine which of the claimed compounds can exhibit antibacterial activity.

It is suggested that in claims 3 and 4, the phrase *of the formula* be used rather than "having the formula".

✧

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 5, 6, 10-12 are rejected under 35 U.S.C. §102(b) as being anticipated by Abbot (USP 4,537,717).

Abbot discloses compound 24 in table III. This compound is encompassed by claim 3 when the substituent variables are as follows:

R = $N(B)(X)_m$-A, wherein

B = hydrogen
X = -CO-
A = alkyl

$R^1$ = $-N(B')(X')_m$-A', wherein

B' = hydrogen
m = 1
X' = CO
A' = t-butoxy

$R^2$ = $-CH_2$-CO- aminophenyl

The claims are anticipated on this basis.

. . . .

Another example is provided by compound 23. This is encompassed by instant claim 3 when the variables are as follows:

R = $N(B)(X)_m$-A, wherein

B = hydrogen
X = -CO-

A = alkyl

$R^1$ = $-N(B')(X')_m-A'$, wherein

B' = hydrogen
m = 1
X' = CO
A' = C12-alkyl

$R^2$ = $-CH_2-CO-$ aminophenyl

It is noted that claim 3 recites that when B' is hydrogen and X' = CO, variable A' is other than $C_1$-$C_{18}$ alkyl, wherein the "alkyl" is optionally substituted with OH, carboxy, alkoxy or halo. However, ambiguity arises because of the definition of the term "alkyl" in the specification. This term is discussed on page 8, last paragraph. As is evident, the term "alkyl" encompasses "substituted alkyl". "Substituted alkyl", in turn, can mean alkyl that is substituted with another alkyl, since alkyl is one of the substituents listed (page 8, 5th line from last). Consider again the following phrase in claim 3:

"variable A' is other than $C_1$-$C_{18}$ alkyl"

One interpretation of the term "$C_1$-$C_{18}$ alkyl" (in claim 3) is that the alkyl (which is excluded from the claims) must be unsubstituted, with the exception that "alkyl" includes "substituted alkyl" if and only if the substituent is OH, carboxy, alkoxy or halo. According to this interpretation, and perversely, the statement that $C_1$-$C_{18}$ unsubstituted alkyl is excluded is actually not effective to exclude $C_{12}$ alkyl. The reason is that $C_{12}$

alkyl can be viewed either as $C_{12}$ unsubstituted alkyl, or else as $C_{11}$ alkyl that is substituted with methyl. Thus, it may be the case that claim 3 would exclude the possibility that A' can be $C_{12}$ unsubstituted alkyl. But it is not clear that claim 3 excludes the possibility that A' can be $C_{11}$ alkyl that is "substituted" with methyl.

Thus, the claims are anticipated.

*

It is suggested that in claims 25-26, the trademark terms be capitalized.

Several of the US Patents have been stricken from the IDS because, in each case, the recited classification is not correct. These have instead been listed on a PTO-892 form with the correct classification.

. . . .

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

D. Lukton

DAVID LUKTON
PATENT EXAMINER
GROUP 1600